1029-22 Catheter-Based Electromechanical Mapping to Assess Myocardial Viability: A Comparative Analysis With SPECT Radionuclide Perfusion Imaging

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Background: Catheter-based assessment of left ventricular (LV) electromechanical activity using a non-fluoroscopic 3D mapping may demonstrate variations in electrical and mechanical activity within regions of infarction or ischemia. This large-scale study examined the correlation between the mapping technique and radionuclide myocardial perfusion imaging.
Methods: A 12-segment comparative analysis model was used in 139 patients (96 males, 63±12 yrs) with refractory angina, having reversible and/or fixed perfusion defects on single photon emission computed tomography perfusion (SPECT) imaging. A dual isotope protocol was used, consisting of rest thallium-201 followed by adenosine technetium-99m sestamibi imaging @stress. Average unipolar voltage (UpV) and local shortening (LS) values were compared with visual-derived perfusion scores and graded on a 0 (normal) through 4 (absent) activity scale within 1668 segments.
Results: There was gradual and proportional reduction in regional UpV and LS in relation to perfusion score @rest and on adenosine stress (p=0.0001 and p=0.0001, respectively, for both comparisons). UpV threshold of >7.4 mV had sensitivity and specificity of 77% and 70% for detecting viable tissue (i.e. perfusion score <2 @rest) with odds and likelihood ratios of 8.1 and 2.6, respectively. UpV of 11.2 and 5.4 mV had 90% specificity and sensitivity, respectively, to predict viable tissue. Receiver-operating characteristic (ROC) curves showed higher sensitivity and specificity for UpV vs. LS value for detecting viability. The area under the curve was greater for rest vs. stress imaging (area under ROC curve was 0.80 vs. 0.61 for UpV, p<0.01, 0.71 vs. 0.60 for LLS, p<0.05).
Conclusion: Catheter based LV electromechanical mapping correlates well with the scintigraphic assessment of myocardial viability, especially as determined by resting thallium imaging.

1029-23 Longevity of the Placebo Effect in Patients Enrolled in Angiogenesis and Laser Myocardial Revascularization Trials

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Background: The investigation of therapeutic angiogenesis and laser myocardial revascularization (LMR) with promising initial phase I open label studies and disappointing negative phase II randomized double blind studies have underscored the role of the placebo effect in this "no-option" patient population. The longevity of this effect, however, has not been defined.
Methods: Patients enrolled in phase I and Phase II angiogenesis and LMR studies (with negative primary endpoints) were followed clinically for persistence of the placebo effect prior to disclosure of trial results and treatment assignment.
Results: A total of 129 patients were so studied. The mean age was 65.4±10 years with 19 women. 46 (36%) patients had Diabetes Mellitus, 40 (31%) had HTN, 112 (87%) had prior CABG, and 57 (44%) had prior myocardial infarction. EF was 44±14% (range: 16-70%). The mean follow-up was 30±6 months (range: 24-42 months). The mean angina class at baseline was 3.0±0.5 (CCS) at baseline and improved to 2.1±0.6 at 6 months (p<0.001) with 24.8% of patients improved by 2 or more angina classes. On long term follow-up, 3 patients (2.3%), 3 (2.3%) patients had a QWMI, and 9 patients (6.9%) had repeat revascularization (PTCA). At last follow-up, the angina class was 2.3±0.8 (p<0.001 compared to baseline and p=0.02 compared to 6-month data) and 26.2% of patients had persistent improvement in 2 or more angina classes. The improvement in Quality of life (SAQ) at 6 months was maintained at last follow-up in 79% of 56 patients studied to date.
Conclusions: The placebo effect observed in many angiogenesis and laser myocardial revascularization studies is mostly maintained at 30±6 months of follow-up. Thus, its persistence cannot be used as evidence of efficacy and double-blinded trials are essential in this patient population.

1029-24 Pilot Study Evaluating the Use of Cryoenergy for Percutaneous Myocardial Revascularization

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Preclinical data in both the canine and porcine model have demonstrated an impressive arteriogenic response in cryo-treated myocardium. In a non-randomized phase II study we evaluated the safety and efficacy of a percutaneous device in humans.
Methods: Patients (n=20) suffering from CCS angina class III or IV not amenable to percutaneous or surgical revascularization were enrolled. Cryoenergy was delivered using a 9F catheter with a 4 mm tip electrode (CryoCath Technologies Inc., Montreal, Canada). The catheter was advanced retrogradely through the aortic valve. Single two-minute cryoapplications were performed at 6 to 8 sites in the left ventricle. Study endpoints included: safety outcomes immediately after the procedure and at 1 month. Efficacy endpoints assessed at 6 months included: Angina class (Canadian Cardiovascular Society score), quality of life index (Seattle angina questionnaire), exercise stress testing (ACIP protocol), and myocardial perfusion (thallium or sesta-mibi nuclear scintigraphy).
Results: The procedure was performed successfully in 18 of 20 patients. Inability to cross a stenotic aortic valve precluded the procedure in one patient. Major complications were encountered in only 1 patient, (pericardial tamponade). Preliminary 6-month data is available for the first 11 of 20 patients. Angina was improved by at least 1 CCS class in all patients and by 2 classes in 64% of patients. The quality of life index was improved in 78% of patients (p<0.05). Exercise times improved in 72% of patients and increased by 1.95 ± 0.81 minutes (p<0.05) at 6 months. However, no significant changes were observed between baseline and 6 month perfusion defects on nuclear scintigraphy.
Conclusions: Percutaneous catheter delivered cryoenergy appears to be a relatively safe procedure. Despite the absence of improvement in myocardial perfusion as assessed by nuclear scintigraphy, preliminary results using this technology are encouraging with a sustained benefit in total exercise times, quality of life and angina class observed at 6 months. Results for all 20 patients are pending and will be disclosed forthcomingly.

1029-25 Adenovirus-Catheter Compatibility Determines Gene Expression Following Delivery to Porcine Myocardium

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Background: Endomyocardial injection of adenoviral gene therapies enables localized delivery to compromised myocardial tissue. In cell culture we have shown that many materials used in endomyocardial delivery catheters are not compatible with adenoviral gene vectors, resulting in up to 90% reduction in virus activity. In this study, we assessed catheter-adenovirus compatibility in an in vivo model.
Methods: In an open chest pig model, using the LAD and LCX as boundaries, the anterolateral epicardial surface was divided into basal and apical regions. A nitinol-stainless steel injection catheter (Ni-SS catheter), or a catheter with a Modified lumen was used to deliver adenovirus (5 injections of 10 ul AdCMV-LacZ, $5x10^9$ IU/ml). To minimize variability, both devices were used in each animal and the injection sequence randomized. Animals (n=4) were sacrificed 3 days post-procedure and the injection zones were dissected. The tissue was homogenized and assayed for β-gal activity and total protein.
Results: Regional β-gal activity expressed as total relative light units (RLU) normalized to total extracted protein was increased in all zones delivered with the Modified catheter.
Conclusions: Fundamental material-virus interactions directly determine efficiency of adenovirus-mediated gene expression in myocardium. These data have important implications for percutaneous myocardial gene delivery.

β-Galactosidase Activity
(RLU/mg protein x 10^5)

Animal	Ni-SS Catheter	Modified Catheter
1	1	17
2	22	450
3	0.2	43
4	30	175

1029-26 Transmyocardial Laser Revascularization and AdVEGF-Transfection Promotes Angiogenesis in Ischemic Myocardium

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Background: The mechanism of transmyocardial laser revascularization (TMR) is unclear. To evaluate the morphologic changes and long-term effects of TMR in chronic ischemia we analyzed vascular density in collateral-dependent myocardium 6 months follwing TMR and/or VEGF transfection.
Methods: An Ameroid constrictor was placed around the left circumflex in 31 pigs. The TMR group (n=9) underwent TMR of the left circumflex territory 6 weeks post-Ameroid. The control group (n=6) had Ameriods without TMR or no operation at all (n=5) or Adenovirus promoted vascular endothelial growth factor (AdVEGF)-transfection, n=6), or combined TMR and AdVEGF-transfection (n=5). Histopathological evaluation by morphometric analysis (IP Lab Spectrum) at 40x and 200x magnification was performed on H&E, CD31, von Willebrand and Anti-VEGF (sc157) stained transmural sections.
Results: Number of vessels (N), vascular density expressed as vascular area (A) and area per vessel (A/N) were measured in the endocardial and epicardial region. Vessel count and vascular density of small vessels (diameter < 500 um) was higher in the endocardial region compared to the epicardial region (N=34+11 vs. N=22+9, p 700 um) were more frequent in the epicardial region compared to the endocardial region and had a higher vascular density (A/N=0.53+0.25 vs. 0.44+0.28, p<0.005). This finding was seen in the TMR group as well as in the controls. In the TMR group, a high vascular density was found in and surrounding the TMR channels compared to myocardium of the same hearts in more than 2 cm distance to the channels (A/N= 0.68+0.31 vs. 0.49+0.24, p<0.001). AdVEGF-transfected endocardial sections revealed A/N= 0.72+0.26 (n.s.), and A/N= 0.95+0.24 (p<0.01) with combined TMR and AdVEGF-transfection.
Conclusions: These data suggest that TMR promotes angiogenesis at the site of intervention in chronic myocardial ischemia. Combinations with growth factors such as VEGF could enhance this angiogenetic effect.